REMARKS/ARGUMENTS

Status of the claims

Claim 17 is under examination, claims 1 and 18-22 have been withdrawn.

Claim 17 has been amended to recite a preparation comprising FVIII:C that is substantially free of platelet agglutinating vWF activity. This amendment adds no new matter. Support can be found, *e.g.,* at page 12, lines 7-11.

Rejection under 35 U.S.C. § 102(b)

Claim 17 remains rejected as allegedly anticipated by SCLAVO, in EP patent EP0600480. The Examiner contends that SCLAVO describes a process for obtaining FVIII:C that includes cation exchange chromatography and step-wise elution at a salt concentration of between >200mM and <300mM. Specifically, the Examiner points to columns 1 and 4 as disclosing a cation exchange step and column 3, second paragraph as disclosing a sodium chloride concentration of 250-350 mM, preferably 300 mM. Applicants respectfully traverse this rejection. EP0600480 does not disclose each of the elements of the claims.

Current claim 17 is drawn to a protein fraction comprising Factor VIII:C obtained from a factor VIII/vWF-containing solution from a cryoprecipitate or recombinant cell where the Factor VIII:C is isolated using cation exchange chromatography and is substantially free of platelet agglutinating vWF activity. In contrast, EP0600480 discloses a Factor VIII:C-vWF complex that is isolated from plasma where the Factor VIIIC-vWF complex is isolated by subjecting plasma to anion exchange chromatography (*e.g.,* column 3, paragraph 13). The FVIII that is adsorbed to the anion exchange resin is eluted with a buffer comprising 0.25-0.35 M sodium chloride. Paragraph 15 discloses that the solution obtained after elution mainly consists of a FVIII:C-FvW complex. The FVIII:C-FvW solution can further be subjected to a viral inactivation process. Such a virus-free solution (obtained after filtration on clarifying membranes) can then be fed into a chromatographic column containing a cationic exchange resin. The adsorbed FVIII:C-FvW complex can then be recovered using TE buffer (paragraph 19). Thus, EP0600480 neither directly nor indirectly discloses a Factor VIII:C preparation that is

free of platelet agglutinating vWF activity. Accordingly, SCLAVO does not anticipate the claim.

Previous rejection of claim 17 for allege indefiniteness over recitation of "substantially free"

Claim 17 as originally presented in Applicants' amendment filed February 23, 2006 was rejected for alleged indefiniteness over the recitation of "substantially free". The Examiner contends that the specification does not provide a definition of "substantially free". This rejection is respectfully traversed. The specification in fact provides guidance for determining a Factor VIII:C substantially free of platelet agglutinating vWF activity. For example, the last sentence of page 7 bridging to page 8 of the specification teaches that free Factor VIII:C and low molecular weight multimers and degradation products are eluted from a cation exchanger at a salt concentration of between ≥250mM and ≤300mM. Page 12 teaches that vWF:C that is substantially free from platelet-agglutinating activity is provided by means of a cation exchange chromatography using stepwise elution at a salt concentration of between ≥200 mM and ≤300mM. The examples, *e.g.*, Table 1 and Table 4, teach that fractions that were eluted from the cation exchangers with 0.3 M NaCl (Table 1) and 0.25 M NaCl (Table 4) did not exhibit measurable vWF:Risto-CoF activity. The vWF:Risto-CoF activity has long been used by those in the art to measure platelet agglutinating vWF activity (see, for example, attached Appendix A, which is an abstract of Weiss *et al., Blood*:45:403-412, 1975).

The fact that claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite. The acceptability of the claim language depends on whether a practitioner of ordinary skill in the art would understand what is claimed, in light of the specification (see, *e.g.*, MPEP § 2173.05(b)). Here the specification provides some standard for measuring the term of degree. Accordingly, the term "substantially free" is definite.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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1: Blood. 1975 Mar;45(3):403-12.

Abnormalities of factor VIII and platelet aggregation--use of ristocetin in diagnosing the von Willebrand syndrome.

Weiss HJ.

Ristocetin was used to study platelet aggregation in platelet-rich plasma and to assay the von Willebrand factor activity of factor VIII (VIII-VWF). Ristocetin-induced platelet aggregation (RIPA) was decreased in 13 of 18 patients with von Willebrand's disease (VWD) who had decreased plasma levels of VIII-VWF. The five patients with normal RIPA appeared to have mild VWD but did not constitute a separate subclass. RIPA was also abnormal in some patients with intrinsic platelet defects, but in no case was the defect corrected by normal plasma. The latter type of correction appears to be specific for VWD. Aspirin ingestion inhibited the second phase of RIPA (at low concentrations of ristocetin only) but did not affect the initial phase of aggregation or the level of VIII-VWF. We also studied a group of patients who had both abnormalities of the factor VIII complex and intrinsic platelet defects, such as impaired collagen-induced aggregation, as well. The findings in these patients and in those with typical von Willebrand's disease appear to comprise a spectrum of disorders (the von Willebrand syndrome) in which some abnormality of the factor VIII complex is associated with impaired platelet function. At present, ristocetin would appear to be a useful reagent for evaluating patients with bleeding disorders and for studying patients with the von Willebrand syndrome.

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Appendix A